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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/911,050	07/23/2001	James L. Bullington	ORT-1477	3229

27777 7590 08/12/2003  
AUDLEY A. CIAMPORCERO JR.  
JOHNSON & JOHNSON  
ONE JOHNSON & JOHNSON PLAZA  
NEW BRUNSWICK, NJ 08933-7003

EXAMINER

ROBINSON, BINTA M

ART UNIT PAPER NUMBER

1625

DATE MAILED: 08/12/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/911,050

Applicant(s)

BULLINGTON ET AL.

Examiner

Binta M. Robinson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 54, 57 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 54, 57 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                             | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____.  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____. | 6) <input type="checkbox"/> Other: _____                                    |

### Detailed Action

(old Rejection)

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 54 and 57 are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement for the method of treating all diseases in claims 54 and 57 many of which are unrelated. The diseases claimed cover such a broad spectrum of diseases that are so unrelated. One drug can not treat various diseases with different mechanisms. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The claims as recited are broader than the scope of enablement.

The applicant is referred to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) which includes the incorporation of the 8 factors recited in *Ex parte* Foreman 230 USPQ 546 (Bd. Of App. And Inter 1986).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is “undue”. These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the

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level of predictability in the art 6) the amount of direction provided by the inventor

7) the existence of working examples, and 8) the quantity of experimentation

needed to make or use the invention based on the content of the disclosure. In

re Wands, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

In terms of the breadth of the claims, R6 of formula I can equal aryl, 3-piperidyl, N-substituted 3-piperidyl, N-substituted 2-pyrrolidinyl methylene, as well as the nonheterocyclic rings claimed, R' and R'' of both formulas I and II can come together to form the heterocyclic rings claimed as well as the non-heterocyclic rings claimed, R1 and R2 of formulas I and II can come together to form oxadiazole, R7 of formulas I and II can be 2-thieno and 3-thieno as well as the non-heterocyclic moieties claimed, R9 of formula II can be cyclic carbonate as well as lactone, and RI and RII can be heterocyclyl optionally substituted with the moieties claimed.

In terms of the nature of the invention, these compounds are useful as calcium channel antagonists with cardiovascular, antiasthmatic and antibronchoconstriction activity.

In terms of the fifth Wands factor, the level of predictability in the art was low since there is large variation in Nitrendipine Binding activity with small changes in structure. For example, compound 3 of formula I in Table 1, differs from compound 6 at the R1 and R5 moieties. In compound 3, R1 is CL and R5 is F. In compound 6, R1 is H, R5 is Cl. For compound 1, Nitrendipine Binding is 160 nM, and for compound 6, Nitrendipine binding is 0.045 nM. Additionally, compounds 2 and 3 appear to have the same structure, however, Nitrendipine binding for compound 2 is 0.043 nM and for compound 3 is 160 nM. The compound have also not been tested for their effects on the specific diseases claimed. In terms of the sixth Wands

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factor, the amount of direction provided by the inventor is poor, because the applicant does not conduct tests for compounds of formulas I and II where R1 and R2 come together to form oxadiazole, where R7 is 2-thieno or 3-thieno or formula II where the substituents on R9 are other optionally substituted heterocyclic rings other than lactone, cyclic carbonate, piperidine, or pyridyl.

The applicant does not test a representative breadth of compounds encompassing the moieties that these particular radicals can be. In terms of the 8<sup>th</sup> Wands factors, undue experimentation would be required to make or use the invention based on the content of the disclosure due to the breadth of the claims, the level of predictability in the art of the invention, and the poor amount of direction provided by the inventor. Taking the above factors into consideration, it is not seen where the instant claim is enabled by the instant application.

(modified rejection)

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 54 and 57 are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement for R' and R'' of formula I coming together to form all of the heterocyclic rings claimed, R1 and R2 of formulas I and II coming together to form an oxadiazole, R' and R'' substituents on R9 of the compounds of formula II independently forming a heterocyclyl, heterocyclyl being optionally substituted with halogen,

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cyano, NO<sub>2</sub>, or lactone. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The claims as recited are broader than the scope of enablement.

The applicant is referred to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) which includes the incorporation of the 8 factors recited in *Ex parte* Foreman 230 USPQ 546 (Bd. Of App. And Inter 1986).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is “undue”. These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art 6) the amount of direction provided by the inventor 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In *re Wands*, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

In terms of the breadth of the claims, R6 of formula I can equal aryl, 3-piperidyl, N-substituted 3-piperidyl, N-substituted 2-pyrrolidinyl methylene, as well as the nonheterocyclic rings claimed, R' and R'' of both formulas I and II can come together to form the heterocyclic rings claimed as well as the non-heterocyclic rings claimed, R1 and R2 of formulas I and II can come together to form oxadiazole, R7 of formulas I and II can be 2-thieno and 3-thieno as well as the non-heterocyclic moieties claimed, R9 of formula II can be cyclic carbonate as well as lactone, and RI and RII can be heterocyclyl optionally substituted with the moieties claimed.

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In terms of the nature of the invention, these compounds are useful as calcium channel antagonists with cardiovascular, antiasthmatic and antibronchoconstriction activity.

In terms of the fifth Wands factor, the level of predictability in the art was low since there is large variation in Nitrendipine Binding activity with small changes in structure. For example, compound 3 of formula I in Table 1, differs from compound 6 at the R1 and R5 moieties. In compound 3, R1 is CL and R5 is F. In compound 6, R1 is H, R5 is Cl. For compound 1, Nitrendipine Binding is 160 nM, and for compound 6, Nitrendipine binding is 0.045 nM. Additionally, compounds 2 and 3 appear to have the same structure, however, Nitrendipine binding for compound 2 is 0.043 nM and for compound 3 is 160 nM. In terms of the sixth Wands factor, the amount of direction provided by the inventor is poor, because the applicant does not conduct tests for compounds of formulas I and II where R1 and R2 come together to form oxadiazole, where R7 is 2-thieno or 3-thieno or formula II where the substituents on R9 are other optionally substituted heterocyclic rings other than lactone, cyclic carbonate, piperidine, or pyridyl.

The applicant does not test a representative breadth of compounds encompassing the moieties that these particular radicals can be. In terms of the 8<sup>th</sup> Wands factors, undue experimentation would be required to make or use the invention based on the content of the disclosure due to the breadth of the claims, the level of predictability in the art of the invention, and the poor amount of direction provided by the inventor. Taking the above factors into consideration, it is not seen where the instant claim is enabled by the instant application.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (703) 306-5437. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alan Rotman can be reached on (703)308-4698. The fax phone numbers for the organization where this application or proceeding is assigned are (703)308-7922 for regular communications and (703)308-7922 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-0193.

Binta Robinson

August 10, 2003



**ALAN L. ROTMAN**  
**SUPERVISORY PATENT EXAMINER**  
**TECHNOLOGY CENTER 1600**